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### MICROSATELLITE MARKERS FOR PLANTS OF THE SPECIES

#### TRITICUM AESTIVUM AND TRIBE TRITICEAE

#### AND THE USE OF SAID MARKERS

BACKGEOUND OF THE INVENTION

The invention relates to novel genetic markers for wheats Triticum.

aestivum Land closely related species (Tribus Triticeae) and to the use of said markers.

The most widely spread, known, DNA-based genetic markers are the so-called restriction fragment length polymorphisms (RFLP) markers. For using these markers, genomic DNA is digested with restriction enzymes, separated on agarose gels and transferred to nylon membranes (Southern Blot). Specific fragments are detected by hybridization with radioactively labeled DNA probes. mutations occur in the region of the restriction enzymes used or when smaller deletions/insertions occur, polymorphisms between different lines are found, which are passed on stably and mostly codominantly. The use of RFLP markers in hexaploid cultivated wheat is possible only to a limited extent, since only very little polymorphism is detected in wheat in this manner.

It has already been described that microsatellite markers detect significantly more polymorphism between different wheat lines than do RFLP markers. This can be attributed particularly to the occurrence of multiple alleles per locus (Röder et al., Mol. Gen. Genet. (1995) 246, 327 - 333). Moreover, it is known that microsatellite markers have the advantage that they can be detected by way of PCR and that therefore large amounts of samples can be analyzed more easily.

SUMMARY OF THE INGUTEON

It is an object of the invention to provide novel microsatellite markers for the genetic analysis of plants of the Triticum aestivum species, which markers are distinguished by a degree of DNA polymorphism, which is higher than that of other molecular probes, that have been developed previously for the wheat genome.

as follows

This objective is accomplished by claims 1 The inventive markers are based on the amplification of certain hypervariable genome sections, the so-called microsatellites, with the help of their polymerase chain reaction (PCR). For specific amplification, two primers, in each to the case left and the right in the flanking sequences, are required for each microsatellite locus. On the average, these primers are  $20 \pm 3$  bases long and are defined by their sequences. In principle, a microsatellite marker is a sequence tagged site (STS), which is defined by two specific primers. These primers flank, in each case to the left and the right, a socalled microsatellite sequence. A microsatellite sequence is defined as a tandem repetitive repetition of a di-, tri- or tetranucleotide sequence, for example (GA)<sub>n</sub>, in which  $n \ge 10$ . Composite microsatellite sequences also occur, such as  $(GT)_n(AT)_n$ , as well as imperfect sequences, in which individual bases are mutated, such as (GA)<sub>n</sub>CA(GA)<sub>n</sub>. Among various lines and varieties, there is variation in the number of repeats at a certain locus. After amplification of the microsatellites, this leads, by means of the specific primers in the flanking sequences, to PCR products of different length and, with that, to polymorphisms. These polymorphisms are passed on stably and can therefore be used as genetic markers. In some cases, null alleles (no visible fragment) also occur, when there are mutations within the binding site for the primers.

The separation and detection of the PCR products obtained can be carried out with different technical variants. For separating the fragments, highly resolving agarose gels, native polyacrylamide gels or denaturing polyacrylamide gels (= sequencing gels) can be used. Depending on the separation system, fragments are detected using ethidium bromide staining, silver staining or, after labeling the PCR

fragments radioactively, using autoradiography. A further, very effective variation for separation and detection consists of the use of an automatic sequencer with dye- or fluorescence-labeled primers. For this purpose, it is necessary to synthesize a dye- or fluorescence-labeled primer from each microsatellite primer pair. PCR amplification results in a labeled product, which can be detected by the sequencing equipment. At the same time, dye- or fluorescence-labeled size standards are also separated for each sample in the same track. After that, special software enable the absolute size of each fragment, which has been separated, to be calculated and, with that, also permits fragments from different gel runs to be compared. With this method, several hundred samples can be analyzed largely automatically in a day.

Pursuant to the invention, microsatellite markers are made available, which contain the following primer pairs with assigned microsatellite sequences or a number thereof and amplify the loci of all chromosomes of the wheat genome and therefore find use for gene marking.

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5' GGC AGA GCA GCG AGA CTC 3'

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5' AAG ATG GAC GTA TGC ATC ACA 3' 5' TCT CCC ATC CAA CGC CTC 3'

5' CTG TTC TTG CGT GGC ATT AA 3'

5' ATT CGA GGT TAG GAG GAA GAG G 3' 5' ATT AAT ACC TGA GGG AGG TGC 3' 5' TCT GTA GGC TCT CTC CGA CTG 3' 5' CGA CAA TGG GGT CTT AGC AT 3' 5' CTA AAC ACG ACA GCG GTG G 3'

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5' TGA CTA ACA TCC TTT GTC ACG C 3' 5' GAT GTT GCC ACT TGA GCA TG 3'

> 3118 3119

5' ACA AAC AGA AAA TCA AAA CCC G 3'

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5' GAT TAT ACT GGT GCC GAA AC 3' 5' CTC GCA ACT AGA GGT GTA TG 3' 5' AAA CCA TCC TCC ATC CTG G 3'
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CAG TAC TTG GTA CTG AAC AGG 3'
S' ACA CTG TCA ACC TGG CAA TG 3'
SI CAT CGG CAA CAT GCT CAT C 3'
SICHT CAC TITC ANG GEGTGA CA 3'
S' ACT CACAAA TGT CTA ATA AAA C3
S' CTC TGG CAT TGC TCC TJG G3.
S' CAA AGC TTG ACT CAG ACC AAA 3
S' CTA GCA TCG AAC CTG AAC AAG 3'
5' TGG TAG AGA AGG ACG GAG AG 3'
S' ATG TGT ACA TGT TGC CTG CA 3'
S' AAT CAT TGG AAA TCC ATA TGC C
S' CAA TGC AGG CCC TCC TAA C 3'
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	5' AAT TTC ACT GCA TAC ACA AG 3'	66
	S' CTG CCC AAT TTT CTC CAC TC 3'	241
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	5' TCT CAT TCA CAC ACA ACA CTA GC 3'	220
TGG 3'	5' GCA CAT TITI TCA CITI TCG GG 3'	123
	S' ATC GAC CGG GAT CTA GCC 3'	243
/	5' AAT GGT ATC TAT TCC GAC CCG 3'	> 158
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CG 3,	S' GCA GAG TGA TCA ATG CCA GA 3'	100
	S' GAC GGC TGC GAC GTA GAG 3'	258
_	5' GCC TAA TAA ACT GAA-AAC GAG 3'	149
	S' TGC GTA AGT CTA GCA TTRICT G 3'	150
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119	131	193	165	231	150	123	187 (225)	801	183	159	132	133 (150)	691	131	203	230	146	E	224	123	164	217	126	249	188	170
LOS AND CCA ACA AGG G 3'		33,		303'	S AUT CAG TTT GCG TTA AGC TTT G 3'	S A A C A TG TGT TTT TAG CTA TC 3'	S ANCINIC AND TIGG TAC CITY TC 3'	S CALC TOT THE TEG TAC TTE CAG G 3'	STATE TAA CTG GCC TTT GCC 3'	S I OC 1711 STORY ACC ACT CAA TC 3'	SI ANG AGG CAA GAA CAC ACA TG 3'	S ACC ACATCT CAT GGA TCC AC 3'	S CCU ACA CTT TGG ACG ACA CC 3'	S DOI CIN CO. TO A BOT ITO CA 3'	S ATT LOS CONTROL OF STANKING	S OCH I S COL TAC CAT CCT ACIT	S AIC COI COO COO COO COO COO COO COO COO C	S CCA L COLOR DAY G CTA CGA AC 3'	S CII GCC CASC	S CCA ATC ACC CTC TTC TTC AG 3'	S AGG CIG CIG CTC ATC TC 3'	STATE TOT TOT GGG ACA ATG G 3'	STACTICATION OF STACE	S ACA ALA ACC ATG AGC TCA CTT GC 3'	s ANT CATE GET GTT GTG AGC 3'	S ACC CIC CCT TGC TTG GTA CC 3'
	5' TCA CAA AAT GAT TTC TCA TCC G 3'	S' TTT CIT CIG TCG TIC TCT TCC C 3'	5' GCA ATC CAC GAG AAG AGA GG 3'	5' TTG CTA TCC ATG TGC CAG AG 3'	S'AGC CAG CAA GTC ACC AAA AC 3'	S' GCC EGG TCA TGT AAA ACG 3'	S' AAT TTC AMA AAG GAG AGA GA S	5' CGT ACT CCA CTC CAC G G S	SI CCC TITI AAT CTC GCT CCC IC 3	5' CCT CTT CCT CCC TCA CTT AGC 3	S' AAT TIT CIT CCI CAC TIA TI 3'	5' GCA ATC TTT TTT CTG ACC ACG 3'	5' TTC AGT GGT AGC GGT CGA G 3'	5' TAT CCA GAG CAG ACG GAC G 3'	5' CAA GGA AAT AGG CGG TAA CT 3'	S' CAA GCA AGG TIT CGT ITF AIC C 3	5' GGC TTC CAG AAA ACA ACA GG 3'	S' ACC TCA TCC ACA TGT TCT ACG 3'	S' CCA TGT TGA GTA GGT TCA GCC 3'	5' AGC GTT CTT GGG AAT TAG AGA 3'	5' TAT GGT CAA AGT TGG ACC TCG 3'	5' AAA CAG CGG ATT TCA TCG AG 3'	5' CTA ATT GCA ACA GGT CAT GGG 3'	5' GTA ACT TGT TGC CAA AGG GG 3'	S' CCA TIT CAC CTA ATG CCT GC 3'	5' CTG CAG GCC ATG ATG ATG 3'

50°C J. 09 55 °C

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55 °C 55 °C 55 °C

CT,CACT,CA

GA,GCGT

GA GA

W	U	y	//U	120

J. 09	2° 55	ე, 09	J. 09	၁. 09	25 °C	၁, 09	၁့ 09	55 °C	25 °C	25 °C	၁, 09	25 °C	၁. 09	25 °C	25 °C	25 °C	25 °C	25 °C	ე. 09	25 °C	၃့ 09	20 °C	၁/ နှာ	/ ၁ <sub>၀</sub> ၀၄	25 °C	၃၈ %	55 °C
GT	CA	CA, GAimp	GA	15	GTimp	CT,CA,CA	CT,GT	CT,GT	CA,GA	CA	CA	CT	CA	CA	CA	CA	CT	GA	GA	GAimp	CT	CA	GA	0) CT	T5	CI	CI
713	156	147	115	195	204	162	130	143	150	107	147	179	139	133	176	334	148		/3	131	>143	215	143	221 (290)	216	109	112
	STECT AAT TAG CGT 1GG C1G CC3	St GGG ATG TCT COTT CCT TCT CTT CTT CTT CTT CTT CT	STILL LLC GOA GOG 1110 CT TTT TG 3'	S' CIA CGI UCA CCA CCA CA	S GAC A 1C TITL CITT AGC TAG TTA A 3'	S GCC AND THE CONTROL AND THE AGC 3'	S CAC COC CITY OF A TANGE CAG AT 3'	S TOC CAL SCIT STATE GAG TCT GC 3'	S TON CAN STITE CO. S. S. A. A. C. T. C. T	SAIG INCLUSION OF A TO THE TOTAL OF A TOTAL	S ICA AND TACTOR AGE CETTED 3'	S. JAC CAA CAC COT TOO A	STOLD AND TOTAL THE GGA G3'	5' Tul Add CAC TOC 115 CT CCA GG 3'	S' AIA AAA CAU I CATT CATT CATT CATT CATT CATT CATT CA	Signature of Section 1978 SA 3'	S' CGA GAL CITI GAG GGI CIA	Si CAA ACCUAA CAT GOT CCCC	S' ATG AAA CUC UAC	S' GAT CGI CIC GIGCLI GOGTIE	S' CGA CAG I CG I CA CT. CCC.	STICULIC ICC CAN COC 15.	S' AUI OIO IIC AII I CII CII CII CII CII CII CII C	STICICCACT ASS SEE	STILL AND CAC CITY CITY OF A LACE A CA A GT GGG ACA 3'	S ACC AAAA TICO TAA GCT TA 3'	S' TCA TGT CAA CTC AAG AAC ACG 3'
	S' ATA GTG TGT TGC ATG CTG TGT G 3'	5' ATT GGC GAC TCT AGC ATA TAC G 3'	5' GGG CTA GAA AAC AGG AAG GC 3'	S' GTC AGA TAA CGC CGT CCA AT 3'	S'ACG CCA GTT GAT CCG TAA AC 3'	S' TTT TCA TTG TGC CCT CTA CT 3'	5' CTA CAA TTC GAA GGA GAG GGG 3'	S' ATC ATG TCG ATC TCC TTG ACG 3'	S' AAG TTT CAC ACA AGA TCT CTC US'	S' ATA GCG AAG TCT CCC TAC TSC A S'	S' TCA TCT GCT ATT TGT GCT ACA 3'	5' TAC AAC CGC AAG TAA TGC CA 3'	5' TGT CAT GGA TTA TTT GGT CGG 3'	5' GTG CTG CCA CCA CTT GC 3'	5' CGA CAT TGG CTT CGG TG 3'	5' TCG ATT TAT TTG GGC CAC TG 3'	5' GCT TGA GAC CGG CAC AGT 3'	5' CCC ATA CGA TGA TGT GTT TCC 3'	5' ATC AAC AAG GTT TGT GTG 'TTG G 3'	5' TGC TTG TCT AGA TTG CTT GGG 3'	5' GAT CTC CCA TGT CCG CC 3'	5' GAG CCC ACA AGC TGG CA 3'	5' AAA CTT AGA ACT GTA ATT TCA GA 3'	5' CGA GGC AGC GAG GAT TT 3'	S' TTG TAC ATT AAG TTC CCA TTA 3'	5' ATG AGT TCC GCC AAA GAA TG 3'	S' GAT CAA GAC TTT TGT ATC TCT CS

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5437 S440 3429 3434 428

5' CCT ATG GTC TCC ATC ATG AGG 3'

110

**80**€

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**AS443 AS445**  **4S458** 

**MS459 MS469** MS471

**AS455 AS456** 

AS-448

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55°C 55°C	وں <sub>د</sub> ر 32 ور	25 °C	J, 09	၁၃ ၄၄ (၅၈ (၄	ე. 09	55 °C	၁. 09	ာ ၁, 09	55 °C	J. 09	၁ ၈ ၁ ၈	55°C	ر د وورد	ာ ၁ ၁	.D. 09	J. 09	25 °C	25 °C		<b>ာ ၈</b> 9	၁. 09	J. 09	55 °C
CA,GA CT	GA	GA	CA	GA CT	CA	GTimp	GAimp	CT, CA	CT	CA	GA	GTimp	QA 5	S E	; చ	GTimp	CA	ر د	GT	CT, CA	CA, TA	GTimp	CTimp
134	231	132	113	>138	149	220	>194	188	145	861	168	>106	145	172		134	166	186	142	147	209	147	129
S' CCA TGA TTT ATA AAT TCC ACC 3'	S' CAC ATG GCA TCA CAT TTG TG 3'	5' ACG GAG AGC AAC CTG CC 3'	5' TTC GCA ATG TTG ATT TGG C 3'	5' AGC TTC TCT GAC CAA CTT CTC G 3'	S' CGA TAA CCA CTC ATC CAT TITT GC 3'	S' CAC CCC CTT GTT GGT CAC 3'	5' TTG CTG GTA GCT TCA ATC CC 3'	S CCG AAT TGT CCG CCA TAG 3'	S' AGT FCC GGT CAT GGC TAG G 3'	S'TIC CTG CTG TCT GGC 3'	4 TGC TTC TGG TOT TCC TTC G 3'	S'CCG AAA GAT GGG TGA TAT AC 3'	S' GGG SAG'TGG AAA CTG CATAA 3'	S' TCC ACA AAC AAG TAG CGC C 3'	S' GAA CAT GAG CAG TITI GUC AC 3	s GGF CTG TTC AIG CCA CALLOS	SCCITICING TAR CICIOS CONTROL STORY	S'CAG GGI GGI GCA 19C 111 3	S'ICA ACI ICI 100 cci cci i cci	STICACITUDES CICUMITATES CONTROL CONTR	S GLI OCI TIA GCG CIII I CII 3	5' GTT GCA TGT ATA CGT TAA GCG G 3'	5' AGG CAT GGA TAG AGG GGC 3'
5' GGG TCT TCA TCC GGA ACT CT 3'	5' TTT GTT GGG GGT TAG GAT TAG 3' 5' AAA CCA TAT TGG GAG GAA AGG 3'	5' ATT CGG TTC GCT AGC TAC CA 3'	5. TCT GAA CAT TAC ACA ACC CIGA 3	5' ATG GAG TGG TCA CAC TTT GAA 3'	S' CAA CTC AGT GCT CAC ACA ACG 3'	5' CGG CCC TAT CAT GGC T63'	S'TCA TAC GGG TAT GGT 190 AC 3		St TGC TGC TAC 11G TAC AGA CGA CF	SI ACA TCG CTC TIC ACA AAC CC3	S' ATT GAA CAU GAA GAC ATC AGG 3'	S' GAG AGC CIC OCO AAA IAI MOOS	5' GIA GIG AAG ACA ACG SCATTS	S' GGC TAT CTC TGG CGC TAA AA 3'	5' AGC CAC CAT CAG CAA AAA TT 3'		5' AAC ACA ATG GCA AAT GCA GA 3'	5' AAT CAC AAC AAG GCG TGA CA 3'	S' AAA TAG GAC AAC CCA CGG C 3'	5' ACT GCG TGT GCC TAC AAT TG 3'	5' AAG GCG AAT CAA ACG GAA TA 3'	S' ACA TAA TGC TTC CTG TGC ACC 3	S' TCT CGC TGT GAA ATC CTA TTT C 3'

VMS540 VMS538

VMS533 VMS537

/MS515 /MS518 /MS530 VMS532

MS512 /MS513

MS501

MS497 MS499

MS495

MS494

MS476

MS473

MS480 MS484

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VMS544	5' TAG AAT TCT TTA TGG GGT CTG C 3'	5' AGG ATT CCA ATC CTT CAA AAT T 3'	167	CT, ATCT, CT 55°C	25°C	
WMS550	5' CCC ACA AGA ACC TTT GAA GA 3'	5' CAT TGT GTG TGC AAG GCA C 3'	150	CT, GT	25 °C	
VMS554	S'TGC CCA CAA CGG AAC TTG 3'	S' GCA ACC ACC AAG CAC AAA GT 3'	160	CT,GTimp	J. 09	
VMS565	S' GCG TCA GAT ATG CCT ACC TAG G 3'	S' AGT GAG TTA GCC CTG AGC CA 3'	142	CA	ე. 09	
VMS566	S' TCT GTC TAG CCA TGG GAT TTG 3'	S' CTG GCT TCG AGG TAA GCA AC 3'	130	CA,TA	J. 09	
VMS569	5' GGA AAC TTA TTGATT GAA AT 3'	5' TCA ATT TTG ACA GAA GAA TT 3'	134	GT	47 °C	
VMS570	5' TCG CCT TTT ACA GTC GGC 3'	5' ATG GGT AGC TGA GAG CCA AA 3'	143	CT, GT	J. 09	
VMS573	5' AAG AGA TAA CAT GCA AGA AA 3'	5' TTC AAA TAT GTG GGA ACT AC 3'	212	CA	20 °C	
VMS577	5' ATG GCA TAA TTT GGT GAA ATT G3'	5' TGT TTC AAG CCC AAC TTC TAT T 3'	133	CA,TA	25 °C	
VMS582	5' AAG CAC TAC GAA AAT ATG AC 3'	S'YCT TAA GGG GTG TTA TCA TA 3'	151	CA	20 °C	
VMS583	5' TTC ACA CCC AAC CAA TAG CA 3'	5' TCT ASG CAG ACA CAT GCC TG 3'	165	CA	J. 09	
VMS588	5' GAT CCC CAA TTG CAT GTT G 3'	5' CTT GCA ACT GGG GGA CAC 3'	102	GT	J. 09	

'CS' Weizensorte 'Chinese Spring'

These markers are distinguished by a high degree of polymorphism between different wheat varieties or lines and usually detect several alleles per genetic locus in different wheat lines.

They can therefore be used for DNA fingerprinting, species identification, relationship or similarity studies, characterization of cytological lines, such as deletion lines, substitution lines, addition lines, etc. and all forms of genetic mappings, including mapping of individual genes and quantitative distinguishing features-(QTLs). In addition, their use is also very suitable for automation and it is possible to carry out the detection of the products with nonradioactive methods.

, With the help of-this-inventive marker, the possibility is provided, for example, of differentiating almost all European wheat lines.

The invention is described in greater detail below by means of examples.

#### 1. Amplification of the Microsatellite Markers

The microsatellite markers are amplified according to the following protocol:

10 mM tris-HCl, pH 8

50 mM KCl

1.5 mM MgCl<sub>2</sub> (in a few exceptional cases 3 mM MgCl<sub>2</sub>)

0.01% (w/v) gelatin

0.2 mM of each desoxynucleotide

250 nM of each primer (in each case to the left and right of a pair)

1 - 2 units taq polymerase

are amplified in a volume of 25 or 50  $\mu$ L according to the following profile:

92°C 3 minute

92°C 1 minute (denaturing phase)

60°C 1 minutes (annealing phase)

45 cycles

72°C 2 minutes (elongation phase)

72°C 10 minutes (extension phase)

The amplification takes place in a Perkin Elmer 9600 with lid heating or in an MJ Research Thermocycler without lid heating. In this apparatus, a layer of mineral oil is placed over the reactions. The temperature of the annealing phase depends on the melting point  $(T_m)$  of the primer and in some cases even is 50°C or 55°C.

# 2. Separation of the Microsatellite Markers on Polyacrylamide Gels, Which Are Not Denaturing

The PCR reactions are mixed with 1/10 volume of stop buffer (0.02 M tris acetate of pH 8.1, 0.025 M sodium acetate, 0.02 M EDTA, 70% glycerin, 0.2% SDS, 0.6% bromphenol blue, 0.6% xylene cyanol) and in each case 25  $\mu$ L are separated in 10% polyacrylamide gels (1.5 mm thick, 18 cm long).

Formulation for polyacrylamide gel (10%):

25 mL stock acrylamide solution (19 g acrylamide, 1 g bisacrylamide, diluted to 100 mL with water)

10 mL 5X TBE (1X TBE = 0.09 M tris borate of pH 8.3, 0.002 M EDTA 15 mL water

are mixed and the polymerization is started by the addition of 220  $\mu$ L of ammonium persulfate (10%, freshly prepared) and 20  $\mu$ L of TEMED. Immediately after the addition, the mixture is poured into the sealed gel mold and the comb for forming pockets is inserted. The polymerization is completed after about 1 hour. The gel is placed in the gel chamber and a preliminary run is carried out without samples for about 30 minutes at 150 volts in 1X TBE. After that, the samples are loaded (25  $\mu$ L of each) and the separation is carried out for 14 - 16 hours at 100 volts.

After the electrophoresis is completed, the gel is stained for about minutes in ethidium bromide (1 - 2 drops of 10 mg/mL in 1 liter of water) and the fragments are made visible by a UV transilluminator and documented.

#### 3. Separation of Microsatellite Markers on Denaturing Gels

For the separation of the amplified fragments on denaturing gels, an automatic laser fluorescence (A.L.F.) sequencer (Pharmacia), for example, is used. In order to enable the fragments to be detected by means of a laser, one primer per pair is marked at the 5' end with fluorescein. Per PCR reaction, 0.3 to 1.5 microliters are mixed with 2.5 microliters of stop buffer (deionized formamide; 5 mg/mL dextran blue), denatured (1 minute; 90°C) and loaded onto the gel. Gel plates with a 9 cm separation distance are used, as recommended by the manufacturer for the fragment analysis. The gel solution contains 6.5% Long-Ranger (AT Biochem), 7M urea and 1.2X TBE buffer. The gels are 0.35 or 0.5 mm thick. The conditions for the gel run are 600 V, 40 mA, 50 W, 0.84 s data collection interval and 2 mW laser energy. The gel runs are ended after about 80 to 90 minutes. This is sufficient for detecting fragments up to a size of 300 bp. A gel can be used for four or five runs. For each gel

run, a data set is obtained. With this data set and by means of internal size standards, the exact fragment sizes are determined in the computer program Fragment Manager (Pharmacia) and thus the smallest size differences of a base pair are determined.

5' TGA CTA ACA TCC TTT GTC ACG C 3'

WMS119

**WMS120** 

WMS121

WMS118

WMS114

WMS113

**WMS112** 

WMSIII

5' GAT GTT GCC ACT TGA GCA TG 3'

5' TCC TCT ACA AAC AAA CAC AC 3'

5' GAT CCA CCT TCC TCT CTC TC 3'

5' ATT AAT ACC TGA GGG AGG TGC 3'

S' CTG TTC TTG CGT GGC ATT AA 3'

WMS106 WMS107 **WMS108** 

5' TCT CCC ATC CAA CGC CTC 3'

5' TCT GTA GGC TCT CTC CGA CTG 3'

5' CTA AAC ACG ACA GCG GTG G 3'

5' CGA CAA TGG GGT CTT AGC AT 3'

5' AAG ATG GAC GTA TGC ATC ACA 3'

5' GAT CAA ACA CAC ACC CCT CC 3'

5' ACG TTA GAA GGT GCA ATG GG 3'

5' CAC TAC AAC TAT GCG CTC GC 3'

5' ACA AAG GTA AGC AGC ACC TG3'

**WMS077** WMS082 WMS088 WMS095 WMS099 WMS102

WMS071

5' GGC AGA GCA GCG AGA-CTC-3'

S-AGT-GGC TGG-GAG AGT GTC AT 3'

5' AGG CCA GAA TCT GGG AAT G 3'

WMS068 PASON W 18

Repeat Type GAA,CA,TA AAAAAimp GT,GAimp Repeat-Typ CA,GA GTimp CT,GT CTimp G CAG E, G GA 5' AAT AAG GAC ACA ATT ÒGG ATG G 3' 5' CAA GTG GAG CAT TAG GTA CAC G 3' 5' GAT TAG TCA AAT GGA ACA CCC C 3' 5' GAA AAA AAT TGC ATA TGA GCC C 3' 5' TGC ACA CTT AAA TTA CAT CCG C 3' 5' CAA CCC TCT TAA TTT TGT TGG G 3' 5' CGA TCA AGT AGT TGA AAG CGC 3' 5' AAT GCA AAG TGA AAA ACC CG 3' 5' GGT CTC AGG AGC AAG AAC AC 3' 5' GAT ATG TGA GCA GCG GTC AG 3' 5' GAG GGT CGG CCT ATA AGA CC 3' 5' CAT GTC TCA ACC ACC CAC AG 3' 5' GAT TAT ACT GGT GCC GAA AC 3' 5' CTC GCA ACT AGA GGT GTA TG 3' 5' ACC TGA TCA GAT CCC ACT CG 3' 5' CTC CCT AGA TGG GAG AAG GG 3' S' GCC ATA TTT GAT GAC GCA TA 3' 5' CGC CCT GGG TGA TGA ATA GT 3' 5" TCC AXT GGC TTC TCT CTC AA 3" STGT TGG TGG CTT GAR TAT TG 3' S' ATC CAT CGC CAT TGG AGT G 3' 5' GCA TTG ACA GAT GCA CAC G 3' 5' TCA TGG ATG CAT CAC ATC CT 3 5' AGT GGA TGC ACC GAC TIT G 3' 5' GCC CAT TAC CGA GGA CAC 3' S' ACC CTC TTG CCC GTG TTG 3' 5' TGC GGT GCT CTT CCA TTT 3' WMS Primer Right WMS Primer rechts 5' ATT CGA GGT TAG GAG GAA GAG G 3' S' ACA AAC AGA AAA TCA AAA CCC G 3'

5' ACC ACA CAA ACA AGG TAA GCG 3'

5' GCA TCT GGT ACA CTA GCT GCC 3'

5' CTA TGA GGC GGA GGT TGA AG 3'

WMS Primer left WMS Primer links

WMS Number VMS-Nummer 5' TCG ATT CTG AAA GGT TCA TCG 3'

5' TCT GAT CCC GTG AGT GTA ACA 3'

VMS058

VMS055 VMS057

**VMS052** 

5' TGT CCT ACA CGG ACC ACG T 3'

5' TCG ACC TGA TCG CCC CTA 3'

VMS063 VMS067

VMS060

VMS159 VMS160 VMS161

VMS162 VMS163 VMS164

7MS157

/MS156

/MS154 /MS155

/MS153

	S' AAA CCA TCC TCC ATC CTG G 3'	CT,CA
S GGG 10G CAC ANN CONTROL CONT	5' ACT GTT CGG TGC AAT TTG AG 3'	CT,GTimp
S OCC ALC CCI TITOTICS CITES	5' GTT GAG TTG ATG CGG GAG G 3'	CA
S CAC ACC CITY TAA CAC AGA TA 3'	5' ATC TGT GAA ATT TTG AAA AC 3'	CA
STATE OF GGC AAG CTA CAC AG 3	5' AAA ACT TAG TAG CCG CGT 3'	GTimp
s AGC TCT GCT TCA CGA GGA AG 3'	5' CTC CTC TTT ATA TCG CGT CCC 3'	GT
S' AAT CCC CAC CGA TTC TTC TC 3'	5' AGT TCG TGG GTC TCT GAT GG 3'	C.
S'TAC CAA ATC GAA ACA CAT CAG G 3'	5' CAT ATC AAG GTC TCC TTC CCC 3'	GA;GAA
5' ATC TAA ACA AGA CGG CGG TG 3'	5' ATC TGT GAC AAC CGG TGA GA 3'	<del>ل</del>
S' CAT GGA ACT TAG ACA GAA TTG 3'	5' CAG TAC TTG GTA CTG AAC AGG 3'	CA
STIGH GAA CAT CGT TITT GAA AAG G 3'	5' ACA CTG TCA ACC TGG CAA TG 3'	ВA
S' GAC AGC ACC TTG CCC TTF 6.3'	5' CAT CGG CAA CAT GCT CAT C 3'	تا تا
5' ATG GAG ATA TTT GGC CTA CAA C 3'	STETT GAC TTE AAG GCG TGA CA 3'	נל
5' TTT GCT GTG GTA CGA AAC ATA C 3'	5' ACT CAC AAA KGT-CSA ATA AAA C 3'	CT :
5' CCA AAA AAA CTG CCT GCA TG 3'	S' CTC TGG CAT TGC TCC TTG GT	GAimp
5' GTG AGG CAG CAA GAG AGA AA 3'	5' CAA AGC TTG ACT CAG ACC AAA3'	CA
5' CAT TGT TTT CTG CCT CTA GCC 3'	5' CTA GCA TCG AAC CTG AAC AAG 3'	e VO^
5' GAT CTC GTC ACC CGG AAT TC 3'	5' TGG TAG AGA AGG ACG GAG AG 3'	В
S'TCA CAG AGA GAG AGG GAG GG 3'	S' ATG TGT ACA TGT TGC CTG CA 3'	QA C
SICAA TCA TTT CCC CCT CCC 3'	5' AAT CAT TGG AAA TCC ATA TGC C 3'	C. L.
S' CCA ACC GTG CTA TTA GTC ATT C 3'	5' CAA TGC AGG CCC TCC TAA C 3'	CI
S' GTC GTC GCG GTA AGC TTG 3'	5' GAG TGA ACA CAC GAG GCT TG 3'	C
S' GGG CCA ACA CTG GAA CAC 3'	5' GCA GAA GCT TGT TGG TAG GC 3'	5
S' TTC AAT TCA GTC TTG GCT TGG 3'	5' CTG CAG GAA AAA AAG TAC ACC C 3'	QΑ
S' GAT CGA GTG ATG GCA GAT GG 3'	5' TGT GAA TTA CTT GGA CGT GG 3'	ב
S' AGT GGA TCG ACA AGG CTC TG 3'	5' AGA AGA AGC AAA GCC TTC CC 3'	CA
S' ACC TCG ACA GAC CTG GTA CG 3'	5' GTC TTT GTC ACC CGA TGG AC 3'	C
5' ACA TTT CTC CCC CAT CGT C 3'	5' TTG TAA ACA AAT CGC ATG CG 3'	ರ

MS146 /MS148 /MS149

'MS136 'MS140 /MS144

MS134

MST35

MS133

MS132

MS131

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MS122 MS124 MS126 MS128 MS130

MS129

WMS210

WMS212 WMS213

WMS205

WMS195 **WMS197** WMS198 WMS200 WMS203

WMS192 WMS193 WMS194

WMS191

WMS186 WMS189 WMS190

WMS182

WMS181

WMS179 WMS180

**VMS165** VMS169 **WMS174**  WMS219 WMS224 WMS228

WMS231

WMS218

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CA,GA CT,CA CT,GT GA CA CT  $C_1$ C CTGA GA IJ IJ GT CT 5' TGC AGT TAA CTT GTT GAA AGG A 3' 5' AAC AGT AAC TCT CGC CAT AGC C 3' 5' TAG CAC GAC AGT TGT ATG CAT G 3' 5' CAA AAT GCA CAA GAA TOG AGG 3' 5' AAT TGT GTT GAT GAT TTG GGG 3' S'EGA EGC AGA ACT TAA ACA AG 3' S' TCA GTT TÀK TTT GGG CAT GTÀ3' S' GAC CTG'ATG ÀBÀ GCA AGC AC 31 5' TGA GAG GAA GGC TCA CAC CT 3' S' CGT TGT CTA ATC TTG CCT TGC 3' 5' GTG CTC TGC TCT AAG TGT GGG 3' 5' CTA GCT TAG CAC TGT CGC CC 3' 5' AGA AAT ACG GAA ACC CAC CC 3' 5' AGT CGC CGT TGT ATA GTG CC 3' 5' CAA CAT CCG CTC GTA TTC AA 3' 5' TTG CAC ACA GCC AAA TAA GG 3' 5' CGC CTC TAG CGA GAG CTA TG 5' 5' GAC ACA CAT GTT CCT GCC AC 3' 5' GAA CCA TTC ATG TGC ATG TC 3' S' GTG TGC CAC CTT TGA CGT C 3' 5' GTG CCA CGT GGT ACC TITT G 3' 5' CCA TGA CCA GCA TCC AC '' C'3' 5' GGG GTC CGA GTC CAC AAC 3' 5' ACC AAT GCT ATC GGC TCG 3' 5' ACC CAC GAC AGA GAG 3' 5' GAT CCG CCG CTG CGT TT 3' 5' GAT CGC ACG GGA GAG AG, 5' TGC ATC AAG AAT AGT GTG GAA G 3' 5' ACC ACT GCA GAG AAC ACA TAC G 3' 5' TCA TAT GCA CCT CTT TCC TAG G 3' S' GGG TTC CTA TCT GGT AAA TCC C 3' 5' GAG AAA GAG GTC TGG AGG TCG 3' 5' TGA TGT AGT GAG CCC ATA GGC 3' 5' GTG CTT GCT GAG CTA TGA GTC 3' 5' TTG AAC CGG AAG GAG TAC AG 3' 5' GAT GAG CGA CAC CTA GCC TC 3' 5' GCA GAG CCT GGT TCA AAA AG 3' S' AAG CAA CAT TTG CTG CAA TG 3' 5' TCA TTG GTA ATG AGG AGA GA 3' 5' AAG TTG AGT TGA TGC GGG AG 3' 5' ATC CGC CTA AGG AAT AGT GT 3' 5' TCA ACG GAA CAG ATG AGC G 3' S' TGC CTG GCT CGT TCT ATC TC 3' 5' TGC AGT GGT CAG ATG TTT CC 3' S' GGT TTF CIT ICA GAT IGC GC 3' 5' GAT CTG CTC TAC TCT CCT CC 3' s' CTT TGT GCA CCT CTC TCT-66.3. 5' AGG AGC AGC GGA ACG AAC 3' 5' CGG CAA ACG GAT ATC GAC 3' 5' AGC TCG GGA TGA AGC GTG 3' 5' TGA GTC CAG CAC TGC TGC 3' 5' AGG TGC CGT CGC GTC TAC 3' 5' AGA CTG TTG TTT GCG GGC 3' S' CGA CCC GGT TCA CTT CAG 3' 5' CCC AAA GCA GCG CAA GC 3'

Harry Brief Com And Con Harl Harry H He was the first that the first that the

S' CTT TTC TTT CAG ATT GCG CC 3'

**6**848430**2** PCT/DE96/01185 21 WO 97/01567 CT, GA 5 QP CP GAIMP ć ₹ C S GTT CAM ANC ANA TTA ANA GGC CC3 G S'TTT GAG CTC CAA AGT GAG TTA GC 3' 5 S'TAT TTG AAG CGG TTT GAT TT 3' E S' AGC AGT GAG GAA GGG GAT C3' 40 S'TTA TOT GAT TOC OTA COT ACC C 3' G. S' AGC TGC TAG CTT TTG GGA CA 3' S' GCA TGC ATG AGA ATA GGA ACT G 3' 5 GAimp CT, GT, GGGT S' GAGTAC ACA TTT GGC CTC TGC 3' 5 Q.P Ś CAimp **₹** S' GOT TTC ATT GCT TGC CCT AA 3' GP IJ S' CTC GCG CTA CTA GCC ATT G 3' Q.P S'CCA AGA COA TOC TORAGT CAT CTICA S, CTG CCA TTT TTC TGG ATC TAC C 3' Q C S'GGG ATGICT GIT CCA TCT TAG 3' S COC AGC TAC AGG AGG CC3' S' CGA CCG ACT TCG GGT TC 3' S. OTA CAC OCCOTA OGC CC31 STOT GCK GTA NOT COC CTC 3 U S'TGG CGT GGT CTA AAT GGA C3' S' CTT CCA TGG ACT ACA TAC TAG C 3' & S S'TGT TGT TGG CCT GTA TGC AT 3' S ATC TOT CCA TTC GAG CGC 3' s, atg tgc atg tcg gac gc 3' S'TCA ACC GTG TGT AAT TTT GTC C 3' S' TTT GGA CAT TTC CCA GCG 3' S CTG GAT GCA TCA CAT CCA AC 3' S, CTC ATT GGG GTG TGT ACG TG 3' S' AGT GCC TTG CCG AGG TC 3' S' CTG ATG CAA GCA ATC CAC C 3' S' TGC ATA TAA ACA GTC ACA CAC CC 3' S' AACTTG CAA AACTGT TCT GA 3' S' ATT GGA CGG ACA GAT GCT TT 3' S' TGC TCT TTG GCG AAT ATA TGG 3' S' AGG GGA TAT GTT GTC ACT CCA 3' S CAA GAT CGT GGA GCC AGC 3' S' GAG AAA CAT GCC GAA CAA CA'' S'TGT TGC GGA TGG TCA CTA TT 3' S AGG GAA AAG ACA TCT TTT TTT TC 3' S CAA CTGTAC GTA GGT TTC ATT GC 3' S' GAT CGC TTC ATC TCT CTC TCT C3' S' CTC CCT GTA CGC CTA AGG C3' S'TCT GCC GTA AGT CGC CTC3' S' CAA CTG GTT GCT ACA CAA GCA3' S GCC CCC TTG CAC AAA TC 3' S' CAA ATG GAT CGA GAA AGG GN T S' AGA GTG CAT GGT GGG ACG 3' S' GCA ATC TTT TTT CTG ACC ACG 3' S' GAA TCA CTT GTG AAG CAT CTG G 3' S'TCA AAA CAT AAA TGT TCA TTG GA 3' S' GAG TCC TGA TGT GAA GCT GTT G 3' S' AGG ACT TCE GCA CCC TG 3' S'TCT TCC AAC TAA AGC ATA GC 3' S' GGC AGC TGA GGC AAT CTG 3' S, CAG CGC AGT TAG CTC GC 3' S' TCC AAG GCA GTA GGC AGG 3' S' TCG CTT CTA CCG CTC ACC 3' SI ATC TCA ACG GCA AGC CG 31 WMS274 WMS273 WMS272 WMS271 WWS269 897SWN NNS265 VMS264 VMS263 yMS261 VMS260 1MS259 1MS258 IMS257 MS255 18251 ,MS249 MS248 WS247 MS245 MS244 MS242 MS241 WS238 WS237 4823N AS233 18232

VMS322

VMS325

/MS316 7MS319 VMS320 VMS321

/MS312 /MS313 /MS314

'MS311

MS304

PCT/DE96/01185

t t	GTimnGAimp	1		GA	GA	СА	CA	CT	CA	GAimp	GA	CT	GT, GA	GA, TAG	GA,G	QA	/ 5	GA	GA	CT,GT	CI	AT,GT	Cł	GT,GA	GT,GAimp	GA	CT
S' AAC AAA AAA TTA GGG CC 3'	S' AAT TTC ACT GCA TAC ACA AG 3	S'CTG CCC AAT 111 CLC CAC 1C 3	5' GCA GGT AAT GGC CGG AC.3'	5' TCT CAT TCA CAC ACA ACA CTA GC 3'	5' GCA CAT TIT TCA CIT TCG GG 3'	5' ATC GAC CGG GAT CTA GCC 3'	5' AAT GGT ATC TAT TCC GAC CCG 3'	5' CCA CCG AGC CGA TAA TGT AC 3'	S' TCG CCA TCA CTC GTT CAA G 3'	5' GCA GAG TGA TCA ATG CCA GA 3'	5' GAC GGC TGC GAC GTA GAG 3'	-5. GCC TAA TAA ACT GAA AAC GAG 3'	S' TGC GTA AGT CTA GCA TITI TCT G 3'	S' TGA CCC ACT TGG AAT TEATC 3'	5' GTG GCT GGA GAT YCA GGT TC3'	s' cag atg ctc ttc tct (ct 60 3)	5' AGG ACT GTG GGG AAT GAA TG 3'	5' CTA CGT GCA CCA CCA TTT TG 3'	5' ACA TGC ATG CCT ACC TAA TGG 3'	5' TTT GAC AAG TAC ACG AGT CTG C 3'	S' TTC GGG ACT CTC TTC CCT G 3'	5' TGC GTG TGG TCC ACC TC 3'	5' CGG GTG CTG TGT GTA ATG AC 3'	5' ATC TTT GCA AGG ATT GCC C 3'	S' TGT TGC ATG CGA TCA TGC 3'	5' TGC AGA AAA CCA ACA AGG G 3'	5' TTT TTA CGC GTC AAC GAC G 3'
5' AAT TIT CIT CCT CAC TTA TTC T 3'	5' ATT TGC CTG AAG AAA ATA TT 3'	5' GTT GCT TCA TGA ACG CTC AA 3'	S' CGG CCA TAT TTC TGT AAG TAT GC 3'	state and Garata AA GGC AG 3'	STIC COCCIO TITE COCCIO SI STIC COCCIO SI	S AAT GAA AAM TOTO CCA AAC AC 3'	A A TO ACC CLI CLO COLLEGE AND A CHARLES AND	S'CAT CCC TAC GCC ACT CTG C 3	STICA CLUING ICA CCU AC 3	STACTION INCACA TIS STACES STATEMENT AND CAST MACCOUNTY	TOTAL TO CAR ACTIVE AND ACTIVE	S'GIG AAG CAC CAC TAIL CIG 3'	5' AAT TCA ACC TAC CAA TCT CTG 5	S' AIC GIC ACG IAI III COMMON	S' ACT ACT TAG GCC TCC CGC CC	S GAG GAG TERN GOOD STORE STORE STORE AND STORE AND AGE AAC AGE AGE AAC AGE	5' AGG AAA CAG AAA TAT CGC GG 3'	S'TCA CGT GGA AGA CGC TCC 3'	STATE GCA TGC ACG TAG AG 3'	si one one tray and the AGT TTC AC 3'	S AGG AGG TCC TCT GTG CCA C 3'	S CAT GGA CAT TTT ACC ACA AGA C 3'	CALCON CIT CAT CIT CAC G 3'	S'GOL TOC TOL ACAMOS CON CONTROL CONTR	S' CGA GAI ACI AIG GAA GGI GGG C	S'CAA IGI GGA GAT GAT TTC TCA TCC G 3'	S' TTT CTT CTG TCG TTC TCT TCC C 3'

MS299

MS301 MS302

MS295 MS296 MS297

**4S276 AS278** 

**4S275** 

**MS293 MS292** 

MS294

AS282 AS284 **4S285 MS291** 

AS281

S' GAC CAA GAT ATT CAA ACT GGC C 3'

5' CTA ATT GCA ACA GGT CAT GGG 3'

5' GTA ACT TGT TGC CAA AGG GG 3'

VMS361

/MS359

S' CCA TTT CAC CTA ATG CCT GC 3'

S' CTG CAG GCC ATG ATG ATG 3'

VMS369

VMS371

/MS368

VMS372 VMS374

5' AAA CAG CGG ATT TCA TCG AG 3'

5' AGC GTT CTT GGG AAT TAG AGA 3' 5' TAT GGT CAA AGT TGG ACC TCG 3'

S' ACC TCA TCC ACA TGT TCT ACG 3' S' CCA TGT TGA GTA GGT TCA GCC 3' S' ATA GTG TGT TGC ATG CTG TGT G 3' S' ATT GGC GAC TCT AGC ATA TAC G 3'

**VMS375** 

S' AAT AGA GCC CTG GGA CTG GG 3'

CT,CACT,CA

S' GTC TCT TTC TCG TAC TTC CAG G 3'

5' CGG TCC AAG TGC TAC CTT TC 3'

S' AAC ATG TGT TTT TAG CTA TC 3'

5' AAT TTC AAA AAG GAG AGA GA 3'

5' GCC CGG TCA TGT AAA ACG 3'

AS333 AS334 AS335 AS336

5' AGC CAG CAA GTC ACC AAA AC 3'

5' TTG CTA TCC ATG TGC CAG AG 3'

5' ACG AGG CAA GAA CAC ACA TG 3'

5' GGT CTA GCT TCG ACG ACA CC 3'

S' CAA GCA AGG TTT CGT TTT ATC C 3'

S' CAA GGA AAT AGG CGG TAA CT 3'

S'TAT CCA GAG CAG ACG GAC G 3'

STITC AGT GGT AGC GGT CGA G 3'

5' GCA ATC TTT TTT CTG ACC ACG 3'

S' AAT TIT CIT CCT CAC TIA IT 3'

MS340 MS341

**MS337** 

S' CCT CTT CCT CCC TCA CTT AGC 3'

S' CCC TIT AAT CTC GCT CCC TC 3'

5' CGT ACT CCA CTC CAC ACG G 3'

5' GGC TTC CAG AAA ACA ACA GG 3'

MS349

MS350

MS346

MS342 MS344 MS353 MS356 MS357 MS358

5' CCG ACA TCT CAT GGA TCC AC 3'

5' AAA CGA ACA ACC ACT CAA TC 3'

5' TGC TAA CTG GCC TTT GCC 3'

GA,GCGT

CT, CTTimp GCGT,GT CA, GA GAimp CTimp GAimp AT,GT GA GT S GA GA GT S' AAT AAA ACC ATG AGC TCA CTT GC 3' 5' GGG ATG TCT GTT CCA TCT TAG C 3' S' TAC TTG TGT TCT GGG ACA ATG G 3' 5' ACA AAG TGG CAA AAG GAG ACA 3' S' GAA GGA CGA CAT TCC ACC TG 3' 5' TCT AAT TAG CGT TGG CTG CC 3' 5' AGC TCA GCT TGC TTG GTA CC 3' 5' ATC GGT GEG TAC CAT CCT AC 3' 5' TCC GCT GTT GTT CTG ATC TC 3'-5' ATT TGA GTC TGA AGT TTG CA 3' 5-GCA TGT GGT CCA TGT ACT GC 3' S' AGG CTG CAG CTC TTC TC AG Ì 5' CTT GGC CAGNAG CTA CGA AC 5' CCA ATC AGC CTÒ CAA CAA G 3' 5' ACC GTG GGT GTT GTG AGC 3' 5' GCA TGG ATA GGA GGC GC 3'

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5' AGT GCT GGA AAG AGT AGT GAA GC 3'

5' CAC AAA CTC TTG ACA TGT GCG 3' 5' ACA TGT TTC ATG CAG GTA GCC 3'

5' GCA ATC CAC GAG AAG AGA GG 3'

4S328 4S330 4S332

S'TTT CAG TTT GCG TTA AGC TTT G 3'

CA, GAimp

S' TITI TCA TTG TGC CCT CTA CT 3'

WMS376

WMS382 **WMS383 WMS384**  24

CT,CA,CA CT,GT CT,GT CA,GA GAilm GT GA IJ 5' CCT TAA CAC TTG CTG GTA GTG A 3' 5' GTA TAA TTC GTT CAC AGC ACG C 3' 5' ACG AAA TAC ACA AGT GGG ACA 3' 5' TCA TGT CAA CTC AAG AAC ACG 3' 5' GCC AAG TIT CTT AGC TAG TTA A 3' 5' CCA TGA TTT ATA AAT TCC ACC 3' 5' GAC ATC AAT AAC CGT GGA TGG 3' 5' CAC CGC GTC AAC TAC TTA AGC 3' 5' CTG CAC TCT CGG TAT ACC AGC 3' 5' GAT GTC CAA CAG TTA GCT TA 3' 5' ATA AAA CAG TGC GGT CCA GG 3' 5' TTT AAG GAC CTA CAT GAC AC 3' S' COA GAC CIT GAG GGT CTA GA 3' 5' CGA CAG TCG TCA CYTT GCC TA 3' 5' AGT GTG TTC ATT TGA CAG TT 3' 5' TGC CAT GCA CAT TAG CAG AT 3' 5' TGA CAA GTA CAC GAG TCT GC 3' 5' TAC CAA CAC CCT AGC CCT TG 3' 5' CTA CGT GCA CCA CTT TG 3' 5' TCA AAT ACA CCA ATG TGC C 3' 5' TGT AGG CAC TGC TTG GGA G 3' S' GAT CGT CTC GRÇ CTT GGČ A'S' S'CAA ACG GAA CAT GGT CCC 3' S' TCG TTC TCC CAA GGC TTG 3' 5' TCT CCC GGA GGG TAG GAG 3' S' TTC TCC ACT AGC CCC GC 3' S' ATG AAA COC GAG CTC CC 34 5' ATG TGC ATG TCG GAC GC 3' 5' AAA CTT AGA ACT GTA ATT TCA GA 3' 5' ATC AAC AAG GTT TGT GTG TTG G 3' S' GAT CAA GAC TIT TGT ATC TCT C 3' 5' ATA GCG AAG TCT CCC TAC TCC A 3' 5' AAG TTT CAC ACA AGA TCT CTC C 3' 5' CCT ATG GTC TCC ATC ATG AGG 3' 5' TTT GTT GGG GGT TAG GAT TAG 3' 5' CTA CAA TTC GAA GGA GAG GGG 3' 5' TTG TAC ATT AAG TTC CCA TTA 3' 5' CCC ATA CGA TGA TGT GTT TCC 3' 5' TGC TTG TCT AGA TTG CTT GGG 3' S' ATG AGT TCC GCC AAA GAA TG 3' S' ATC ATG TCG ATC TCC TTG ACG 3' 5' TCA TCT GCT ATT TGT GCT ACA 3' 5' TGT CAT GGA TTA TTT GGT CGG 3' 5' GGG TCT TCA TCC GGA ACT CT 3' 5' TAC AAC CGC AAG TAA TGC CA 3' 5' GGG CTA GAA AAC AGG AAG GC 3' S' GTC AGA TAA CGC CGT CCA AT 3' S' ACG CCA GTT GAT CCG TAA AC 3'

5' TCG ATT TAT TTG GGC CAC TG 3

**WMS403 WMS408** WMS410 WMS411 WMS412 WMS413

WMS400

5' GTG CTG CCA CCA CTT GC 3' S' CGA CAT TGG CTT CGG TG 3'

WMS395 WMS397

WMS393

WMS390

WMS391

WMS388 **WMS389**  5' GCT TGA GAC CGG CAC AGT 3'

5' GAG CCC ACA AGC TGG CA 3'

5' GAT CTC CCA TGT CCG CC 3'

WMS415

**WMS425** WMS427

S' CGA GGC AGC GAG GAT TT 3'

**WMS428 WMS429** WMS434

**WMS445** WMS437 WMS440 WMS443

CT, GT

5' CAT TGT GTG TGC AAG GCA C 3'

PCT/DE96/01185

CT, ATCT, CT CA, TA CT, CA CTimp GTimp GTimp GAimp GTimp CT, CA GTimp GA CA Ϋ́ CA GT IJ CA 5' GTT GCA TGT ATA CGT TAA GCG G 3' 5' AGG ATT CCA ATC CTT CAA AAT T3' S' CCT TCC TAG TAA GTG YGC CYCA 3' 5' AGC TTC TCT GAC CAA CTT CTC G 3' 5' GTT GCT TTA GGG GAA AAG CC 3' 5' GGG GAG TGG AAA CTG CAT AA 3' S' GAA CAT BAQ CAGATT GGC AC 3' 5' GCC ACT TTT GTG TCG TTC CT 3' 5' GGT CTG TTC ATG CCA CAT TG 3' 5' CGA TAA CCA CTC ATC CAC ACC 3' 5' CCG AAA GTT GGG TGA TAT AC 3' 5' TCA ACT TCT TGG CCT CCA TC 3' 5' TCA CTC GCA CTC GAT AGG C 3' 5' TGC TCT CTC TGA ACC TGA AGC 3' STCC ACA AAC AAG TAG CGC C 3' 5' AGG CAT GGA TAG AGG GGC 3' 5' TTG CTG GTA GCT TCA ATC CC 3' 5' GCT TGC AAG TTC CAT TTT GC 3' 5' AGT TCC GGT CAT GGC TAG G 3' 5' CAC ATG GCA TCA CAT TTG TG 3' S' TGC TTC TGG TGT TCC TTC G 3' S' TTC GCA ATG TTG ATT TGG C 3' 5' CCG AAT TGT CCG CCA TAG 3' 5' TTC CTG GAG CTG TCT GGC 3' 5' CAG GGT GGT GCA TGC AT'3' 5' CAC CCC CTT GTT GGT CAC 3' 5' ACG GAG AGC AAC CTG CC 3' S'TCT CGC TGT GAA ATC CTA TTT C 3' 5' ATT GAA CAG GAA GAC ATC AGG G3' 5' TGC TGC TAC TTG TAC AGA GGA C 3' 5' ACT TGT ATG CTC CAT TGA TT6-G3' 5' ATG GGT TCG TAC TAA CAT CAG C 3' S' AAT GGC AAT TGG AAG ACA TAG C 3' S' ACA TAA TGC TTC CTG TGC ACC 3' 5' TCT GAA CAT TAC ACA ACC CTG A 3' 5-GAG AGC CTC GCG AAA TAT AGG 3' 5' ATC CGT AGC ACC TAC TGG TCA 3' 5' AAG GCG AAT CAA ACG GAA TA 3' 5' AAC ACA ATG GCA AAT GCA GA 3' 5' AAT CAC AAC AAG GCG TGA CA 3' 5' ATG GAG TGG TCA CAC TTT GAA 3' 5' ACT GCG TGT GCC TAC AAT TG 3' 5' GTA GTG AAG ACA-AGG GCA TT 3' 5' AGC CAC CAT CAG CAA AAA TT 3' 5' AAA CCA TAT TGG GAG GAA AGG 3' S' CAA CTC AGT GCT CAC ACA ACG 3' 5' GGC TAT CTC TGG CGC TAA AA 3' 5' AAA TAG GAC AAC CCA CGG C 3' 5' TCA TAC GGG TAT GGT TGG AC 3' 5' ACA TCG CTC TTC ACA AAC CC3' 5' ATT CGG TTC GCT AGC TAC CA 3'

> /MS495 /MS497

MS494

MS480 MS484

924SM MS473

5' CGG CCC TAT CAT GGC TG 3'

69FSIM MS471

**AS456 42458 MS459** 

1S448 **VS455** 

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5' TAG AAT TCT TTA TGG GGT CTG C 3' 5' CCC ACA AGA ACC TTT GAA GA 3' 5' GCA TTT CGG GTG AAC CC 3' WMS544 WMS550 WMS538 WMS540 VMS515 WMS533 WMS537 VMS513 WMS518 WMS530 WMS532 VMS512 /MS499 VMS501

**WO** 97/01567

26

GT CT, GT CA CA,TA CA,TA CA S' TGT TTC AAG CCC AAC TTC TAT T 3' 5' ATG GGT AGC TGA GAG CCA AA 3' 5' TTC AAA TAT GTG GGA ACT AC 3' 5' TCT AGG CAG ACA CAT GCC TG 3' 5' TCT TAA GGG GTG TTA TCA TA 3' S' GCA ACC ACC AAG CAC AAA GT 3' 5' TCA ATT TTG ACA GAA GAA TT 3' 5' AGT GAG TTA GCC CTG AGC CA 3' 5' CTG GCT TCG AGG TAA GCA AC 3' 5' CTT GCA ACT GGG GGA CAC 3'

5' AAG CAC TAC GAA AAT ATG AC 3' 5' TTC ACA CCC AAC CAA TAG CA 3' 5' GAT CCC CAA TTG CAT GTT G 3'

S' ATG GCA TAA TTT GGT GAA ATT G 3' 5' GCG TCA GAT ATG CCT ACC TAG G 3' 5' AAG AGA TAA CAT GCA AGA AA 3' 5' TCT GTC TAC CCA TGG GAT TTG 3' 5' GGA AAC TTA TTG ATT GAA AT 3' 5' TGC CCA CAA CGG AAC TTG 3' 5' TCG CCT TTT ACA GTC GGC 3'

> MS569 MS570

MS566

/MS588

MS583

MS582 MS573 MS577

CT,GTimp

MS565 **MS554**